Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE Under the paperwork Reduction Act of 1995, no persons required to respond to a collection of information unless it contains a valid OMB control

				Complete if Known		
Substitute for	Substitute for form 1449/PTO			Application Number	10/733,532	
INFORMATION DISCLOSURE			OSURE	Filing Date	December 11, 2003	
	STATEMENT BY APPLICANT			First Named Inventor	Julian Edward SALE	
(Use as	many shee	ts as nec	essary)	Art Unit	1636	
				Examiner Name	Daniel M. Sullivan	
Sheet	1	Of	13	Attorney Docket Number	33547-731.302	

		U.S. P	ATENT DOC	UMENTS	
Examiner Initials*	Cite No. <sup>1</sup>	Document Number  Number-Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
/D.S./	1.	US-5,750,335	05-12-1998	Gifford	A Igares Tippear

	FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>1</sup> – Number <sup>4</sup> – Kind Code <sup>3</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T	
/D.S./	2.	WO-1995-12689 A1	05-11-1995	Gene Check Inc.			
/D.S./	3.	WO-1993-12228 A1	06-24-1993	Pasteur Institut			

		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the	_
Examiner Initials*	Cite No. '	item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
/D.S./	4.	ADETUGBO, K. et al., "Molecular analysis of spontaneous somatic mutants," Nature 265:299-304 (1977)	
/D.S./	5.	BAHLER, D.W. and LEVY, R., "Clonal evolution of a follicular lymphomas: Evidence for antigen selections," PNAS USA 89:6770-6774 (1992)	
/D.S./	6.	BASS, S. et al., "Hormone Phage: An Enrichment Method for Variant Proteins With Altered Binding Properties," Proteins 8:309-314 (1990)	

Examiner	· ·	Date	
1		Date	
Signature	<b>I</b>	Considered	
		Considered	L

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). 'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 'Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

				Complete if Known		
Substitute for form 1449/PTO				Application Number	10/733,532	
INFORMATION DISCLOSURE			LOSURE	Filing Date	December 11, 2003	
	STATEMENT BY APPLICANT			First Named Inventor	Julian Edward SALE	
(Use a	s many shee	ts as nec	essary)	Art Unit	1636	
			Examiner Name	Daniel M. Sullivan		
Sheet	2	Of	13	Attorney Docket Number	33547-731.302	

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Té
/D.S./ 7.		BEREK, C. and MILSTEIN, C., "The dynamic nature of the antibody repertorie," Immunol. Rev. 105:5-26 (1988)	
	8.	BETZ, A.G., et al., "Elements Regulating Somatic Hypermutation of an Immunoglobulin K Gene: Critical Role for the Intron Enhancer/Matrix Attachment Region," Cell 77:239-248 (1994)	
	9.	BETZ, A.G. et al., "Discriminating intrinsic and antigen-selected mutational hotspots in immunoglobulin V genes," Immunol. Today 14:405-411 (1993)	
	10.	BEZZUBOVA, O. et al., "Reduced X-ray resistance and homologous recombination frequencies in a RAD54-/-mutant of the chicken DT40 cell line," Cell 89:185-193 (1997)	
	11.	BONFIELD, J.K. et al., "A new DNA-sequence assembly program," Nucleic Acids Res. 23:4992-4999 (1995)	
	12.	BOUVET, J.P. and DIGHIERO, G., "From natural polyreactive autoantibodies to a la carte monoreactive antibodies to infectious agents: is it a small world after all?" Infect. Immun. 66:1-4 (1998)	
/D.S./	13.	BRAEUNINGER, A. et al., "Hodgkin and Reed-Sternberg cells in lymphocyte predominant disease represent clonal populations of germinal center-derived tumor B cells," PNAS USA 94:9337-9342 (1997)	

Examiner	Date
	Date
Signature	Considered
	Considered

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 'Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 23313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE Under the paperwork Reduction Act of 1995, no pe

				Complete if Known		
Substitute for form 1449/PTO			,	Application Number	10/733,532	
INFORMATION DISCLOSURE			OSURE	Filing Date	December 11, 2003	
STATEMENT BY APPLICANT		First Named Inventor	Julian Edward SALE			
(Use as	s many shee	ts as nece	ssary)	Art Unit	1636	
				Examiner Name	Daniel M. Sullivan	
Sheet	3	Of	13	Attorney Docket Number	33547-731.302	

	<del></del>		NON PATENT LITERATURE DOCUMENTS	
	ixaminer Cite Initials* No. I Include name of the authorise (book, magazine, jo		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Т
/D.S./ 14. BR		4.	BRENNEMAN, M.A. et al., "XRCC3 is required for efficient repair of chromosome breaks by homologous recombination," Mutat. Res. 459:89-97 (2000)	
	15	5.	BROSS, L. et al., "DNA double-strand breaks in immunoglobulin genes undergoing somatic hypermutaion," Immunity 13:589-597 (2000)	
	16	6.	BRUGGEMANN, M. et al., "Immunoglobulin V region variants in hybridoma cells. I. Isolation of a variant with altered idiotypic and antigen binding specificity," EMBO J. 1:629-634 (1982)	
	17	7.	BUERSTEDDE, J. et al., "Light chain gene conversion continues at high rate in an ALV-induced cell line, Embo J. 9:921-927 (1990)	
	18	8.	CAPIZZI and JAMESON, "A table for the estimation of the spontaneous mutation rate of cells in culture," Mutat. Res. 17:147-148 (1973)	
	, 19	9.	CASALI, P. and SCHETTINO, E.W., "Structure and function of natural antibodies," Curr. Top. Microbiol. Immunol. 10:167-179 (1996)	
<b>∀</b> /D.:	S./ 20	0.	CHAPMAN, C.J. et al. "Analysis of VH genes used by neoplastic B cells in endemic Burkitt's lymphoma shows somatic hypermutation and intraclonal heterogeneity," Blood 85:2176-2181 (1995)	

Examiner		Date	
	•	Date	1
Signature			<u>.</u>
Digitature		Considered	· · · · · · · · · · · · · · · · · · ·
ATT VALATATED			

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 'Ekind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE Under the paperwork Reduction Act of 1995, no persons required to respond to a collection of information unless it contains a valid OMB control n

	•			Complete if Known		
Substitute for form 1449/PTO INFORMATION DISCLOSURE				Application Number	10/733,532	
			OSURE	Filing Date	December 11, 2003	
STATEMENT BY APPLICANT		First Named Inventor	Julian Edward SALE			
(Use as	s many shee	ts as nece	essary)	Art Unit	1636	
		Examiner Name	Daniel M. Sullivan			
Sheet	4	Of	13	Attorney Docket Number	33547-731.302	

	· · · · · · · · · · · · · · · · · · ·	NON PATENT LITERATURE DOCUMENTS					
Examiner Cite No.1  /D.S./ 21.		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.					
		CHAPMAN, K.B. and SZOSTAK, J.W., "In vitro selection of catalytic RNAs," Curr. Op. Struct. Biol. 4:618-622 (1994)					
	22.	CHUI, Y.L. et al., "A reporter gene to analyse the hypermutation of immunoglobulin genes," J. Mol. Biol. 249:555-563 (1995)					
	23.	CLACKSON, T. and WELLS, J.A., "In vitro selection from protein and peptide libraries," Trends Biotechnol. 12:173-184 (1994)					
	24.	COFFINO, P. and SCHARFF, M.D., "Rate of somatic mutation in immunoglobulin production by mouse myeloma cells," PNAS USA 68:219-223 (1971)					
	25.	CUI, X. et al., "The XRCC2 and XRCC3 repair genes are required for chromosome stability in mammalian cells," Mutat. Res. 434:75-88 (1999)					
	26.	CULL, M.G. et al., "Screening for receptor ligands using large libraries of peptides linked to the C terminus of the lac repressor," PNAS USA 89:1865-1869 (1992)					
	27.	DEANS, B. et al., XRCC2 is required for genetic stability, embryonic neurogenesis and viability in mice," Embo J. 19:6675-6685 (2000)					
/D.S./	28.	DENEPOUX, S. et al., "Induction of somatic mutation in a human B cell line in vitro," Immunity 6:35-46 (1997)					

Examiner	Date	
Signature	·	
Signature	Considered	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 'For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.' Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

check mark here if English language Translation is attached.
This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE Under the paperwork Reduction Act of 1995, no pe

				Complete if Known		
Substitute for form 1449/PTO				Application Number	10/733,532	
INFORM	<b>IATION</b>	DISCL	OSURE	Filing Date	December 11, 2003	
STATEMENT BY APPLICANT			ICANT	First Named Inventor	Julian Edward SALE	
(Use as	s many shee	ts as nece	ssary)	Art Unit	1636	
				Examiner Name	Daniel M. Sullivan	
Sheet	5	Of	13	Attorney Docket Number	33547-731.302	

	Ţ	NON PATENT LITERATURE DOCUMENTS  Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the	Г	
Examiner Initials*	Cite No.1	item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number publisher, city and/or country where published.		
/D.S./	29.	DIAZ, M. et al., "Evolution and the molecular basis of somatic hypermutation of antigen receptor genes," Philos. Trans. R. Soc. Lond. B Biol. Sci. 356:67-72 (2001)		
	30.	DRAKE, J.W., "Rates of spontaneous mutation," Genetics 148:1667-1686 (1998)		
	31.	ELLINGTON, A.D. and SZOSTAK, J.W., "In vitro selection of RNA molecules that bind specific ligands," Nature 346:81822 (1990)		
	32.	GOLD, L. et al., "Diversity of Oligonucleotide Functions," Annual Rev. Biochem. 65:763-797 (1995)		
	33.	GONZALEZ-FERNANDEZ and MILSTEIN, "Analysis of somatic hypermutation in mouse Peyer's patches using immunoglobulin κ light-chain transgenes," PNAS USA 90:9862-9866 (1993)		
	34.	GOOSSENS, T. et al., "Frequent occurrence of deletions and duplications during somatic hypermutation: Implications for oncogenic translocations and heavy chain disease," PNAS USA 95:2463-2468 (1998)		
/D.S./	35.	GOYENECHEA, B. et al., "Cells strongly expressing Igk transgenes show clonal recruitment of hypermutation: a role for both MAR and the enhancers," Embo J. 16:3987-3994 (1997)		

Examiner	Date	
1	25440	
Signature	Considered	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 699. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). 'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 'Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

3876695\_1.DOC

check mark here it English language Translation is attached.
This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

				Complete if Known		
Substitute for form 1449/PTO INFORMATION DISCLOSURE				Application Number	10/733,532	
				Filing Date	December 11, 2003	
STATEMENT BY APPLICANT				First Named Inventor	Julian Edward SALE	
(Use as	many shee	ts as nece	ssary)	Art Unit	1636	
				Examiner Name	Daniel M. Sullivan	
Sheet	6	Of	13	Attorney Docket Number	33547-731.302	

		NON PATENT LITERATURE DOCUMENTS			
Examiner Cite It No. 1  /D.S./ 36. G		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s) publisher, city and/or country where published.			
		GREEN, N.S. et al., "Immunoglobulin hypermutation in cultured cells," Immunol. Rev. 162:77-87 (1998)			
	37.	GREEN, N.S. et al., "IG V Region Hypermutation in B Cell Hybrids Mimics In Vivo Mutation and Allows for Isolation of Clonal Variants," Mol. Immunol. 34(15):1095-1103 (1997)			
	38.	GREEN, R. and SZOSTAK, J.W., "Selection of a Ribozyme That Functions as a Superior Template in a Self-Copying Reaction," Science 258:1910-1915 (1992)			
	39.	GRIFFIN, C.S. et al., "Mammalian recombination-repair genes XRCC2 and XRCC3 promote correct chromosome segregation," Nat. Cell Biol. 2:757-761 (2000)			
	40.	JAIN, R. et al., "A potential role for antigen selection in the clonal evolution of Burkitt's lymphoma," J. Immunol. 153:45-52 (1994)			
	41.	JOHNSON, R.D. et al., "Mammalian XRCC2 promotes the repair of DNA double-strand breaks by homologous recombination," Nature 401:397-399 (1999)			
/D.S.	42.	JOLLY, C.J. et al., "Rapid methods for the analysis of immunoglobulin gene hypermutation: application to transgenic and gene targeted mice," Nuceic Acids Research 25(10):1913-1919 (1997)			

Examiner	Date
Signature	Considered

<sup>\*</sup>Signature | Considered |

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). 'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 'Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Approved for use through 07/31/2006: OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE Under the paperwork Reduction Act of 1995, no persons required to res

				Complete if Known		
Substitute for form 1449/PTO				Application Number	10/733,532	
INFORM	<b>MATION</b>	DISC	LOSURE	Filing Date	December 11, 2003	
STATEMENT BY APPLICANT			LICANT	First Named Inventor	Julian Edward SALE	
(Use a.	s many shee	ts as nec	essary)	Art Unit	1636	
				Examiner Name	Daniel M. Sullivan	
Sheet	7	Of	13	Attorney Docket Number	33547-731.302	

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T⁰
/D.S./ 43.		JOLLY, C., et al., "The targeting of somatic hypermutation," Semin. Immunol. 8:159-168 (1996)	
	44.	JOYCE, G.F., "In vitro evolution of nucleic acids, "Curr. Op. Struct. Biol. 4:331-336 (1994)	
	45.	KALLBERG, E. et al., "Somatic mutation of immunoglobulin V genes in vitro," Science 271:1285-1289 (1996)	
	46.	KIM, S. et al., "Ongoing diversification of the rearranged immunoglobulin light-chain gene in a bursal lymphoma cell line," Mol. Cell Biol. 10:3224-3231 (1990)	
	47.	KLEIN, G. et al., "An EBV negative cell line established from a American Burkitt lymphoma; receptor characteristics, EBV infectability and permanent conversion into EBV-positive sublines by in vitro infection," Intervirology 5:319-334 (1975)	
	48.	KLIX et al., "Multiple sequences from downstream of the Jx cluster can combine to recruit somatic hypermutation to a heterologous, upstream mutation domain," Eur. J. Immunol. 28:317-326 (1998)	
/D.S./	49.	LIU, N. et al., "XRCC2 and XRCC3, new human Rad51-family members, promote chromosome stability and protect against DNA cross-links and other damages," Mol. Cell 1:783-793 (1998)	

Examin	CT	Date	
Signatu	-p		
Signatu		Considered	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. Applicant's unique citation designation number (optional). See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. Applicant is to place a check mark here if English language Translation is attached.

check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE Under the paperwork Reduction Act of 1995, no persons required to respond to a collection of information unless it contains a valid OMB control.

				Complete if Known		
Substitute f	or form 144	9/PTO		Application Number	10/733,532	
INFORMATION DISCLOSURE				Filing Date	December 11, 2003	
STATEMENT BY APPLICANT				First Named Inventor	Julian Edward SALE	
(Use as	many shee	ts as neces	ssary)	Art Unit	1636	
				Examiner Name	Daniel M. Sullivan	
Sheet	8	Of	13	Attorney Docket Number	33547-731.302	

		NON PATENT LITERATURE DOCUMENTS					
Examiner Cite No. 1  /D.S./ 50.		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of t item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(publisher, city and/or country where published.					
		LUNDBERG, K.S. et al., "High-fidelity amplification using a thermostable DNA polymerase isolated from Pyrococcus furiosus," Gene 108:1-6 (1991)					
	51.	LURIA and DELBRECK, "Mutations of bacteris from virus sensitivity to virus resistance," Genetics 28:491-511 (1943)					
	52.	MAIZELS, N., "Somatic hypermutation: how many mechanisms diversity V region sequences?" Cell 83:9-12 (1995)					
	53.	MATTHEAKIS, L.C. et al., "An in vitro polysome display system for identifying ligands from very large peptide libraries,"PNAS USA 91:9022-9026 (1994)					
	54.	MATTHIAS et al., "Eukaryotic expression vectors for the analysis of mutant proteins," NAR 17:6418 (1989)					
	55.	MAX, EE. et al., "The Nucleotide Sequence of a 5.5-kilobase DNA Segment Containing the Mouse k Immunoglobulin J and C Region Genes," J. Biol. Chem. 256:5116-5120 (1981)					
	56.	McCAFFERTY, J. et al., "Phage antibodies: filamentous phage displaying antibody variable domains," Nature 348:552-554 (1990)					
/D.S./	57.	McCORMACK, W.T. et al., "Germ line maintenance of the pseudogene donor pool for somatic immunoglobulin gene conversion in chickens," Mol. Cell Biol. 13:821-830	٠				

Examiner	Date	
Signature	Considered	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto gov or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 'Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE Under the paperwork Reduction Act of 1995, no persons required to respond to a collection of information unless it contains a valid OMB control number.

			•	Complete if Known		
Substitute for form 1449/PTO				Application Number	10/733,532	
INFORMATION DISCLOSURE				Filing Date	December 11, 2003	
STATEMENT BY APPLICANT			LICANT	First Named Inventor Julian Edward SALE		
(Use as	s many shee	ts as nec	essary)	Art Unit	1636	
				Examiner Name	Daniel M. Sullivan	
Sheet	9	Of	13	Attorney Docket Number	33547-731.302	

Examiner Cite Initials* No.1		publisher, city and/or country where published.					
		(1993)					
/D.S./ 58.		McKEAN, D. et al., "Generation of antibody diversity in the immune response of BALB/c mice to influenza virus haemagglutinin," PNAS USA 81:3180-3184 (1984)					
	59.	MOORE, M.J., "Exploration by lamp light," Nature 374:766-767 (1995)					
	60.	MU-QUAN, M. et al., "Sequence dependent hypermutation of the immunoglobulin heavy chain in cultured B cells," PNAS USA 94:5284-5289 (1997)					
	61.	NEUBERGER, M.S. and MILSTEIN, C., "Somatic hypermutation," Curr. Op. Immunol. 7:248-254 (1995)					
stra		PAPAVASILIOU, F.N. and SCHATZ, D.G., "Cell-cycle-regulated DNA double-stranded breaks in somatic hypermutation of immunoglobulin genes," Nature 408:216-221 (2000)					
	63.	PARHAM, P. ed., Immunol. Reviews. Somatic hypermutation of immunoglobulin genes, Volume 162, April 1998 (Copenhagen, Denmark: Munksgaard)					
$\bigvee$	64.	PIERCE, A.J., et al., "XRCC3 promotes omology-directed repair of DNA damage in mammalian cells," Genes Dev. 13:2633-2638 (1999)					
/D.S./	65.	RADA, C. et al., "Hot spot focusing of somatic hypermutation in MSH2-deficient mice					

Examiner	Date	
Signature	Consid	dered

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 'Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Approved for use through 07/31/2006. OMB 0651-0031 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the paperwork Reduction Act of 1995, no persons required to respond

1				Con	mplete if Known
Substitute for form 1449/PTO				Application Number	10/733,532
INFORM	MATION I	DISC	LOSURE	Filing Date	December 11, 2003
STATEMENT BY APPLICANT			LICANT	First Named Inventor	Julian Edward SALE
(Use a	s many sheet:	s as nec	essary)	Art Unit	1636
				Examiner Name	Daniel M. Sullivan
Sheet	10	Of	13	Attorney Docket Number	33547-731.302

		,	NON PATENT LITERATURE DOCUMENTS			
Examiner Cite Initials* No.1			Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s) publisher, city and/or country where published.			
			suggests two stages of mutational targeting," Immunity 9:135-141 (1998)			
/D.S./ 66.		66.	RATECH, H., "Rapid cloning of rearranged immunoglobulin heavy chain genes from human B-cell lines using anchored polymerase chain reaction," Biochem. Biophys. Res. Commun. 182:1260-1263 (1992)			
		67.	REYNAUD, C.A., et al., "A hyperconversion mechanism generates the chicken light chain preimmune repertoire," Cell 48:379-388 (1987)			
		68.	REYNAUD, C.A. et al., "Somatic hyperconversion diversifies the single V <sub>H</sub> gene of the chicken with a high incidence in the D region," Cell 59:171-183 (1989)			
69.		69. ROGOZIN, I.B. and KOLCHANOV, N.A., "Somatic hypermutation of immunoglobulin genes. II. Influence of neighbouring base sequences on mutagenesi Biochem. Biophys. Acta 1171:11-18 (1992)				
_	,	70.	ROONEY, C.M., "Paired Epstein-Barr virus-carrying lymphoma and lymphoblastoid cell lines from Burkitt's lymphoma patients: comparative sensitivity to non-specific and to allo-specific cytotoxic responses in vitro," Int. J. Cancer 34:339-348 (1984)			
/D	.S./	71.	ROWE, M. et al., "Differences in B cell growth phenotype reflect novel patterns of Epstein-Barr virus latent gene expression in Burkitt's lymphoma cells," Embo J. 6:2743-2751 (1987)			

Examiner	Date	
Signature	 Considered	
APMARABIED -	 ·	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). 'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.' Skind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Approved for use through 07/31/2006. OMB 0651-0031

				Coi	nplete if Known
Substitute for form 1449/PTO				Application Number	10/733,532
INFORMATION DISCLOSURE				Filing Date	December 11, 2003
STATE	STATEMENT BY APPLICANT			First Named Inventor	Julian Edward SALE
(Use a	s many sheet	ts as nec	cessary)	Art Unit	1636
				Examiner Name	Daniel M. Sullivan
Sheet	11	Of	13	Attorney Docket Number	33547-731.302

		NON PATENT LITERATURE DOCUMENTS						
Examiner Cite Initials* No.1		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of titem (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(publisher, city and/or country where published.						
/D.S./	72. SALE, J.E. and NEUBERGER, M.S., "TdT-accessible breaks are scattered over the immunoglobulin V domain in a constitutively hypermutating B cell line," Immunit 9:859-869 (1998)							
	73.	SHARPE et al., "Somatic hypermutation of immunoglobulin $\kappa$ may depend on sequences 3' of $C\kappa$ and occurs on passenger transgenes," Embo J. 10:2139-2145 (1991)						
	74.	SMITH, G.P., "Filamentous Fusion Phage: Novel Expression Vectors that Display Cloned Antigens on the Virion Surface," Science 228:1315-1317 (1985)						
		TAKATA, M. et al., "The Rad51 paralog Rad51B promotes homologous recombinational repair," Mol. Cell Biol. 20:6476-6482 (2000)						
	76.	TAKATA, M. et al., "Homologous recombination and non-homologous end-joining pathways of DNA double-strand break repair have overlapping roles in the maintenance of chromosomal integrity in vertebrate cells," Embo J. 17:5497-5508 (1998)						
	77.	TAKATA, M. et al., "Chromosome Instability and Defective Recombinational Repair in Knockout Mutants of the Five Rad51 Paralogs," Mol. Cell Biol. 21:2858-2866 (2001)						
/D.S./	78.	TOMLINSON, I.M. (1997). V Base database of human antibody genes. Medical Research Council, Centre for Protein Engineering, UK Confirmation Number: 149990 <a href="http://www.mrc-cpe.cam.ac.uk/">http://www.mrc-cpe.cam.ac.uk/</a>						

			_ •
Examiner		Date	
Signature	<u>.                                    </u>	Considered	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. Applicant's unique citation designation number (optional). See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. Applicant is to place a check mark here if English language Translation is attached.

check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Approved for use through 07/31/2006. OMB 0651-0031 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the paperwork Reduction Act of 1995, no persons required to respond to a collection of inform

				Coi	nplete if Known
Substitute for form 1449/PTO				Application Number	10/733,532
INFORM	<b>IATION</b>	DISC	LOSURE	Filing Date	December 11, 2003
STATEMENT BY APPLICANT			LICANT	First Named Inventor	Julian Edward SALE
(Use a	s many sheet	ts as nec	essary)	Art Unit	1636
				Examiner Name	Daniel M. Sullivan
Sheet	12	Of	13	Attorney Docket Number	33547-731.302

	NON PATENT LITERATURE DOCUMENTS							
Examiner Cite Initials* No.		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(single publisher, city and/or country where published.						
/D.S./	79.	TUERK, C. and GOLD, L., "Systematic Evolution of Ligands by Exponential Enrichment: RNA Ligands to Bacteriophage T4 DNA Polymerase," Science 249:505-510 (1990)						
	80.	WABL, M. et al., "Hypermutation at the immunoglobulin heavy chain locus in a pre-B-cell line, "PNAS USA 82:479-482 (1985)						
	WAGNER, S.D. et al., "Codon bias targets mutation," Nature 376:732 (1995)							
82. WEILL, J.C. and REYNAUD, C.A., "Rearrangement/hypermutaiton/gene convers when, where and why?" Immunol. Today 17:92-97 (1996)								
	83.	WILSON, P.C. et al., "Somatic hypermutation introduces insertions and deletions into immunoglobulin V genes," J. Exp. Med. 187:59-70 (1998)						
·	84.	WU, H. and KAARTINEN, M., "The Somatic Hypermutation Activity of Follicular Lymphoma Links to Large Insertions and Deletions of Immunoglobulin Genes," Scand. J. Immunol. 42:52-59 (1995)						
	85.	WU, H. et al., "A human follicular lymphoma B cell line hypermutates its functional immunoglobulin genes in vitro," Eur. J. Immunol. 25:3263-3269 (1995)						
/D.S./	86.	YAMAGUCHI-IWAI, Y. et al., "Homologous recombination, but not DNA repair, is						

Examiner	Date	
Signature	Considered	·

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST .3). 'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 'Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST .16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Approved for use through 07/31/2006, OMB 0651-0031 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the paperwork Reduction Act of 1995, no persons required to respond to a collection of information unless it contains a valid OMB control number.

•		Complete if Known			
Substitute for	or form 144	9/PTO		Application Number	10/733,532
INFORM	IATION	DISCL	OSURE	Filing Date	December 11, 2003
STATEMENT BY APPLICANT				First Named Inventor	Julian Edward SALE
(Use as	many sheet	ts as nece	ssary)	Art Unit	1636
·				Examiner Name	Daniel M. Sullivan
Sheet	13	Of	13	Attorney Docket Number	33547-731.302

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	1
		reduced in vertebrate cells deficient in RAD52," Mol. Cell Biol. 1:6430-6435 (1998)	
/D.S./ 87.		YELAMOS, J. et al., "Targeting of non-Ig sequences in place of the V segment by somatic hypermutation," Nature 376:225-229 (1995)	
	88.	ZHANG, L. et al., "The development of anti-CD79 monoclonal antibodies for treatment of B-cell neoplastic disease," Ther. Immunol. 2:191-202 (1995)	
	89.	ZHU, M. et al., "A well-differentiated B cell line is permissive for somatic mutation of a transfected immunoglobuin heavy-chain gene," PNAS USA 92:2810-2814 (1995)	
/D.S./	90.	ZOU, X. et al., "Subtle differences in antibody responses and hypermutation of $\lambda$ light chains in mice with a disrupted $\chi$ constant region," Eur. J. Immunol. 25:2154-2162 (1995)	

Examiner	/Daniel M Sullivan/	Date		
Signature	7 Dartier for Sullivary	Considered	09/25/2007	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 'Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Approved for use through 07/31/2006. OMB 0651-0031

				Con	nplete if Known
Substitute	for form 144	9/PTO		Application Number	10/733,532
INFOR	MATION	DISC	LOSURE	Filing Date	December 11, 2003
STATE	STATEMENT BY APPLICANT (Use as many sheets as necessary)			First Named Inventor	Julian Edward SALE
(Use				Art Unit	1636
				Examiner Name	Daniel M. Sullivan
Sheet	1	Of	4	Attorney Docket Number	33547-731.302

		NON PATENT LITERATURE DOCUMENTS				
Examiner Cite No.1  /D.S./ 1.						
		ANDERSSON, K. et al., "Affinity selection and repertoire shift: paradoxes as a consequence of somatic mutation?" Immunological Reviews 162:173-182 (1998)				
	2.	AZUMA, T., "Somatic hypermutation in mouse λ chains," Immunological Reviews 162:97-105 (1998)				
	3.	BLANDEN, R. et al., "The signature of somatic hypermutation appears to be written into the germline IgV segment repertoire," Immunological Reviews 162:117-132 (1998)				
		DIAZ, M. and FICJNIK, M., "Evolution of somatic hypermutation and gene conversion in adaptive immunity," Immunological Reviews 162:13-24 (1998)				
	5.	DORNER, T. et al., "Analysis of the targeting of the hypermutational chemistry and theimpact of subsequent selection on the distribution of nucleotide changes in human V <sub>H</sub> DJ <sub>H</sub> rearrangements," Immunological Reviews 162:161-171 (1998)				
$\bigvee$	6.	GREEN, N. et al., "Immunoglobulin hypermutation in cultured cells," Immunological Reviews 162:77-87 (1998)				
		HSU, E., "Mutation, selection, and memory in B lymphocytes of exothermic vertebrates," Immunological Reviews 162:25-36 (1998)				

Examiner	Date	
Signature	Considered	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto gov or MPEP 901.04. 'Benter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). 'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 'Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the correleted application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the paperwork Reduction Act of 1995, no persons required to respond to a collection of information unless it contains a valid OMB control number.

				Coi	mplete if Known
Substitute f	or form 1449	PTO		Application Number	10/733,532
INFORM	1ATION	DISC	LOSURE	Filing Date	December 11, 2003
STATE	STATEMENT BY APPLICANT			First Named Inventor	Julian Edward SALE
(Use as	s many sheet	s as ne	cessary)	Art Unit	1636
				Examiner Name	Daniel M. Sullivan
Sheet	2	·Of	4	Attorney Docket Number	33547-731.302

		NON PATENT LITERATURE DOCUMENTS	,			
Examiner Initials*	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s) publisher, city and/or country where published.					
/D.S./	S./ 8. KLEIN, U. et al., "Somatic hypermutation in normal and transformed human B cells," Immunological Reviews 162:261-280 (1998)					
	9. KNIGHT, K. and BARRINGTON, R., "Somatic diversifictation of IgH genes in rabbit, Immunological Reviews 162:37-47 (1998)					
	10. KONG, Q. et al., "Recombination-based mechanisms for somatic hypermutation," Immunological Reviews 162:67-76 (1998)					
	KOSMAS, C. et al., "Somatic hypermutation of immunoglobulin variable region gene focus on follicular lymphoma and multiple myeloma," Immunological Reviews 162:281-292 (1998)					
	12. LOPEZ, O. et al., "A single V <sub>H</sub> family and long CDR3s are the targets for hypermutation in bovine immunoglobulin heavy chains," Immunological Reviews 162:55-66 (1998)					
	13.	MAGE, R., "Diversification of rabbit V <sub>H</sub> genes by gene-conversion-like and hypermutation mechanisms," Immunological Reviews 162:49-54 (1998)				
MANSER, T. et al., "The roles of antibody variable region hypermutation and select in the development of the memory B-cell compartment," Immunological Reviews 162:183-196 (1998)						

Examiner	Date	
Signature	Considered	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). 'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.' Skind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

	-	,		Coi	mplete if Known
Substitute f	or form 1449	9/PTO		Application Number	10/733,532
INFORM	IATION :	DISC	LOSURE	Filing Date	December 11, 2003
STATE	STATEMENT BY APPLICANT			First Named Inventor	Julian Edward SALE
(Use as	s many sheet	s as ne	cessary)	Art Unit	1636
				Examiner Name	Daniel M. Sullivan
Sheet	3	Of	4	Attorney Docket Number	33547-731.302

	<del></del>	NON PATENT LITERATURE DOCUMENTS					
Examine Initials		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.					
/D.:	S./ 15.	McINTOSH, R. et al., "Somatic hypermutation in autoimmune thyroid disease," Immunological Reviews 162:219-231 (1998)					
	16.	NEUBERGER, M. et al., "Monitoring and interpreting the intrinsic features of somatic hypermutation," Immunological Reviews 162:107-116 (1998)					
	17.	NG, V. and McGRATH, M., "The immunology of AIDS-associated lymphomas," Immunological Reviews 162:293-298 (1998)					
	18.	SONG, H. et al., "Antibody feedback and somatic mutation in B cells: regulation of mutation by immune complexes with IgG antibody," Immunological Reviews 162:211-218 (1998)					
	19.	STEVENSON, F. et al., "Insight into the origin and clonal history of B-cell tumors as revealed by analysis of immunoglobulin variable region genes," Immunological Reviews 162:247-259 (1998)					
$\downarrow$	STORB, U., "Progress in understanding the mechanism and consequences of somati hypermutation," Immunological Reviews 162:5-11 (1998)						
/D.S.	<i>j</i> 21.	SLORB et al., "Cis-acting sequences that affect somatic hypermutation of Ig genes," Immunological Reviews 162:153-160 (1998)					

Examiner	Date	
Signature	Consi	idered

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). 'For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.' Xind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the paperwork Reduction Act of 1995, no persons required to respond to a collection of information unless it contains a valid OMB control number.

•				Complete if Known			
Substitute for form 1449/PTO INFORMATION DISCLOSURE				Application Number	10/733,532		
				Filing Date	December 11, 2003		
STATEMENT BY APPLICANT (Use as many sheets as necessary)			LICANT	First Named Inventor	Julian Edward SALE		
			cessary)	Art Unit	1636		
				Examiner Name	Daniel M. Sullivan		
Sheet	4	Of	4	Attorney Docket Number	33547-731.302		

	<del></del>	NON PATENT LITERATURE DOCUMENTS	,		
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Té		
/D.S./	22.	WIENS, G. et al., "Harmful somatic mutations: lessons from the dark side," Immunological Reviews 162:197-209 (1998)			
	23.	WILSON, P. et al., "Amino acid insertions and deletions contribute to diversify the human Ig repertoire," Immunological Reviews 162:143-151 (1998)			
	24.	WINTER, D. and GEARHART, P., "Dual enigma of somatic hypermutation of immunoglobulin variable genes: targeting and mechanism," Immunological Reviews 162:89-96 (1998)			
	25.	WYSOCKI, L. et al., "Somatic origin of T-cell epitopes within antibody variable regions: significance to monoclonal therapy and genesis of systemic autoimmune disease," Immunological Reviews 162:233-246 (1998)			
/D.S./	26.	ZHENG, B. et al., "Immunoglobulin gene hypermutation in germinal centers is independent of the RAG-1 V(D)J recominase," Immunological Reviews 162:133-141 (1998)			

Examiner	/D1-1 M O - (P /	Date	09/25/2007	
Signature	/Daniel M Sullivan/	Considered	09/23/2007	İ

<sup>\*\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 'Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 'Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Tradernark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

12/11/03

USPTO Form 1449 U.S. Department of Commerce Patent and Trademark Office			Attorney Docket No. Serial No.						
INFORMATION DISCLOSURE STATEMENT				18396/2002B			2		
				Applicant(s):. Sale et a	al				
<u> </u>				Filing Date: December	Group: Not assigned		s <del>signe</del> d		
U.S. PAT	ENT DO	CUMENTS	·						
Examiner Initial		Patent No.	Date	Name	Class	Subclass	Filing Date (if appropriate)		
DE	1	6,146,894	November 14, 2000	Nicolaides et al	435	440	April 14, 1998		
					_				
				,					
			·						
FOREIGN	N PATE	NT DOCUMENTS							
Examiner Initial		Document No.	Publication Date	Country	Class	Subclass	Translati	on	
			·				YES	NO	
<del>88</del>	2	WO 00/22111	April 20, 2000	PCT	C12N	15/10		x	
	<del></del>			·	<u> </u>	,			
					.				
	<del></del> .								
OTHER I	OCUM	ENTS (including A	uthor, Title, Date, Pertin	ent Pages, etc.)					
#8	3	Mage, Diversificat	tion of a Rabbit V <sub>H</sub> Gen	es by Gene-Convers	ion-Like ar	nd Hyperm	nutation		
DO	4		Mechanisms, Immunogical Review, vol.162, April 1998, pages 49-54  International Search Report PCT/GB02/02688 (2003)						
		Zironian Generi Chapati Chapati Chapati Carana							
	<u>-</u>				<del>-</del>				
EXAMIN	ER A	CO	<del></del>		DATE CO	ONSIDERED	\$ 11/	1	
*EXAMINER: L next communicat	nitial if referen	nce considered, whether or not cit	nation is in conformance with MPEP 609.	Draw line through citation if not i	in conformance an	d not considered.	Include copy of this	S/QS form with	
••Copies of refer	ences not pro-	vided at the time of this submission	na.		•				